

Prevalence of Bronchial Asthma Among Orang Asli in Peninsular Malaysia

R Ngui*, Y A L Lim, PhD*, S C Chow**, J A de Bruyne***, C K Liam****

*Department of Parasitology, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia, **School of Science, Monash University, Jalan Lagoon Selatan, Bandar Sunway, 46150 Selangor Darul Ehsan, Malaysia, *** Department of Pediatrics, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia, **** Department of Medicine, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia

SUMMARY

A survey was carried out to determine the prevalence of bronchial asthma and their contributing risk factors among Orang Asli subgroups living in Malaysia using IUATLD questionnaire and spirometry without being discriminatory towards age or gender. Of the 1171 distributed questionnaires, 716 (61.1%) comprising of 62.7% Semai Pahang, 51.3% Temiar, 74.2% Mah Meri, 65.6% Semai Perak, 53.6% Temuan, 53.8% Semelai, 61.1% Jakun and 67.4% Orang Kuala subgroups completed their questionnaire and were included in the data analysis. Participants comprised 549 (76.7%) children and 167 (23.3%) adults, age between 1 to 83 years old, 304 (42.5%) males and 412 (57.5%) females. The overall prevalence of bronchial asthma was 1.4% of which 1.5% was children, 1.3% adults, 1.0% male and 1.7% female, respectively. Of the 8 subgroups surveyed, 5 out of 10 confirmed asthma cases were Semai Pahang, followed by 3 cases among Mah Meri, and one case each among Temuan and Semai Perak subgroups, respectively. This study also demonstrated that the prevalence of self-reported and confirmed bronchial asthma tend to be higher among those who had close contact with pets, smoking individuals and among those who had a family history of asthma.

KEY WORDS:

Lung function test, Bronchial asthma, Orang Asli, Peninsular Malaysia

INTRODUCTION

Asthma is an important chronic disease and a significant public health problem. Prevalence of asthma is on the rise in all regions of the world, affecting all ages but more commonly among children. There seemed to be a prevalence variation among countries and even within the same country. It is now estimated that as many as 300 million people of all ages and ethnic backgrounds suffer from asthma and the burden of this disease to governments, health care systems, families, and patients is overwhelming¹. In the Asia-Pacific region, the prevalence of asthma is generally lower than those reported in Western countries as revealed by the International Study of Asthma and Allergies in Childhood². The 12 months prevalence of wheezing in teenagers in the Asia-Pacific region is less than half of that reported in Western Europe, being 8.0% and 16.7%, respectively^{2,3}. Asthma mortality rates in

more affluent areas in the Asia-Pacific region, such as Hong Kong and Japan, are similar to those reported in Western countries¹.

In Malaysia, asthma is among the commonest medical conditions treated in health clinics giving rise to considerable morbidity and mortality⁴. More than 73% of outpatient attends in the health clinics have been managed for respiratory symptoms and asthma is one of the cases note to be treated in health clinics⁵. It is estimated that there are about 1.6 to 2 million asthmatics in Malaysia and these figures have been increasing over the years⁶. Hospitalization and mortality due to asthma were also reported to be on the rise in the period from 1990 to 1995⁵. The Second Malaysian National Health and Morbidity Survey (NHMS II) conducted in 1996 has shown that the prevalence of asthma among general Malaysian population was 4.5% and 4.1% in children and adults, respectively. It also revealed that 9.9% and 2.7% of the asthma cases were moderate and severe forms that required hospitalization, respectively⁶. People with asthma suffer illness for about 3.7 to 4.6 days during each asthma attack. This translates into lost of productivity and quality of life for 2.4 days per episode⁶.

Although prevalence of asthma among the Malaysian general population is known^{5,6}, information on asthma among Orang Asli is extremely limited as currently there is neither available publication nor a comprehensive study which has been carried out among these communities. Documented data on asthma are currently non-existent among these communities (personal communication with Ministry of Health, Malaysia). Given the importance of chronic asthma disease and scarcity of available information on asthma among this community, therefore this study was initiated to investigate the prevalence of bronchial asthma among Orang Asli communities. To the best of our knowledge, this is the first available documented data on the epidemiology of bronchial asthma in these communities.

MATERIALS AND METHODS

Study design and area

A cross-sectional study was carried out from November 2007 to July 2009 among 8 villages from 5 different states in rural and remote areas of Malaysia without being discriminatory

This article was accepted: 20 March 2011

Corresponding Author: Yvonne Lim, University of Malaya, Department of Parasitology, Faculty of Medicine, Kuala Lumpur, 50603 Malaysia
Email: limailian@um.edu.my

towards age or gender. Villages include RPS Pos Betau (Kuala Lipis, Pahang), RPS Kuala Betis (Gua Musang, Kelantan), Sungai Bumbun (Pulau Carey, Selangor), Sungai Perah (Parit, Perak), Gurney (Hulu Yam, Selangor), RPS Pos Iskandar (Bera, Pahang), RPS Bukit Serok (Rompin, Pahang) and finally RPS Sungai Layau (Kota Tinggi, Johor). The villages were selected based on (i) village entry approval by the Ministry of Rural and Regional Development Malaysia and (ii) willingness to participate by the head and community members of the villages. The study population consisted of both children and adults. The study presented here used two surveys: first, a questionnaire survey using standardized International Union against Tuberculosis and Lung Disease (IUATLD) questionnaire and second, a lung function test by spirometry.

IUATLD Questionnaire

Before the commencement of the study, an oral briefing explaining the objectives of the study was given to the participants and voluntary written informed consent was taken from each participant. Before the questionnaire interview began, a short video clip on asthmatic symptoms based on the International Study of Asthma and Allergies in Childhood questionnaire² was shown to the participants. The purpose of this short video presentation was to reinforce onto the participants what constitutes asthma. Thereafter, the IUATLD Bronchial Symptoms Questionnaire (1984)⁷ was used to elicit information from participants face-to-face by trained field assistants. Questionnaire encompassed information on basic demographic data details and asthma related variables such as respiratory status and lifestyle. Initially, the questionnaires were constructed in the English language which was later translated into Bahasa Malaysia, which is the national language for Malaysia and well understood by the participants. To maintain the meaning, appropriate linguistic adoptions were made. It concentrated on past and current wheezing episodes, wheezing frequency, sleep disturbances, exercise induced wheezing, persistent coughs unrelated to respiratory infections and a doctor's diagnosis of asthma. Current anti-asthma medication and medical history of participants were also recorded. Some risk factors that may affect the prevalence of asthma such as family history of asthma, passive smoking and presence of domestic animals (e.g. cats and dogs) at home were also taken into consideration.

Pulmonary function test via PC Spirometry (SCHILLER SP-260)

Participants who had symptoms of asthma based on the IUATLD questionnaire or who had self-reported asthma were examined for their lung function test using SCHILLER SP-260 spirometer (SCHILLER AG, Baar, Switzerland) (P/No.2.200 551) to confirm the diagnosis of bronchial asthma. In brief, a spirometric manoeuvre began by entering the subject's demographic data including age, height and gender. These values were needed for the programme in the spirometer to calculate the predicted normal spirometric values. Both of the forced expiratory volume in 1 second (FEV₁) and the forced vital capacity (FVC) was recorded and FEV₁/FVC ratio was calculated. The FEV₁/FVC ratio was used to determine the presence of airflow obstruction typical of asthma while the percent predicted for the FEV₁ was used to indicate the severity of airflow obstruction if present. An obstructive pattern affects the rate at which air can be expelled from the

lung and is characterized by a reduced FEV₁, a reduced FVC and a FEV₁/FVC ratio below 0.7. The recorded values were referred to as pre-bronchodilator measurements.

Following the pre-bronchodilator measurement, the participant was asked to inhale 400 µg of salbutamol, a short-acting bronchodilator, which constituted 4 puffs of salbutamol from a metered dose inhaler at 100 µg per puff. Twenty to thirty minutes following the inhalation of 400 µg of salbutamol, the spirometry test was repeated to evaluate the response to the bronchodilator administration. Again, the best values of the FEV₁ and the FVC from two reproducible manoeuvres were recorded. A 12% or more increase in FEV₁ accompanied by a minimum absolute increase in the FEV₁ value by at least 200 mL confirms reversibility of airflow obstruction and confirms the diagnosis of asthma. The significant increase in FEV₁ following inhalation of a short-acting bronchodilator is indicative of a positive response to a bronchodilator and not a change in the airway size due to normal fluctuation. Both spirometry test and salbutamol administration were carried out by trained medical and field assistants. The spirometry results were validated by the University Malaya Medical Centre (UMMC) consultant respiratory physician.

Statistical analysis

Descriptive analysis was performed on participants' socio-demographic details, asthma-related variables, prevalence of bronchial asthma. These values were described as percentage (rate). The potential risk factors relating to asthma such as age, gender, animals kept in the home, family history of asthma and smoking habit were also assessed. Initial data entry was cross-checked by two independent individuals in order to be sure that data were entered correctly. Before each analysis, data were again checked for consistency. All computation were made using statistical SPSS software (Statistical Package for the Social Sciences) programme for windows version 13 (Chicago, IL, USA).

Ethical considerations

The study protocol (Reference Number: 638.36) was approved by the Ethics Committee of the University Malaya Medical Centre (UMMC), Malaysia before the commencement of the study. Before participating in the study, parents and their children were given an oral briefing by the investigator on the etiology, objective and methodology of the study. The participants were also informed that the procedure used did not pose any potential risk and their identity and personal particular will be kept strictly confidential. During the meetings, parents and their children were informed that their participation was voluntarily and therefore they could withdraw from the study at any point of time without giving any reason whatsoever. If they agreed to participate, their consent were taken either in written form (signed) or verbally followed by their thumb print (for those who are illiterate) from the participants themselves and their parents or guardians (on behalf of their children).

RESULTS

Of the 1171 distributed questionnaires, 716 (61.1%) of participants completed their questionnaires and were included in the data analysis. This of 62.7% Semai Pahang

(RPS Pos Betau, Pahang), 51.3% Temiar (RPS Kuala Betis, Kelantan), 74.2% Mah Meri (Sungai Bumbun, Selangor), 65.6% Semai Perak (Parit, Perak), 53.6% Temuan (Hulu Yam, Selangor), 53.8% Semelai (RPS Pos Iskandar), 61.1% Jakun (RPS Bukit Serok) and 67.4% Orang Kuala (RPS Sungai Layau). With regards to age groups, there were a total of 549 (76.7%) children and 167 (23.3%) adults ranging from 1 to 83 years with mean age of 9.89 ± 2.02 years (mean \pm SD) and 36.34 ± 13.78 (mean \pm SD) and a proportion of 1.1%, 2.4%, 73.3%, 2.0% and 21.2% for the age groups 1 to 4, 5 to 6, 7 to 12, 13 to 17 and above 18 years, respectively. These participants consisted of 304 (42.5%) male and 412 (57.5%) female. As wheeze and cough were the most efficient indicator for the diagnosis of asthma based on questionnaire assessment⁷, these two parameters were evaluated in association with asthma cases. Results of wheezing and coughing as well as cases of self-reported asthma based on the IUATLD questionnaire by age showed that 6.3% (45 of 716) had wheezing in the past 12 months (Table I). Meanwhile, 10.6% (76 of 716) of the participants complained of cough (which often got worse at night) in the past 12 months.

A total of 1.4% (10 of 716) of the participants had self-reported asthma and currently on medication based on their medical records. Wheezing tended to be more common among children age of 12 years and below (8.0%, 44 of 549) compared to adults age of 13 years and above (6.6%, 11 of 167). The prevalence of cough was uniformly distributed among all ages but very high among children aged between 1 and 6 years. As for self-reported asthma, children aged 5 to 6 years (17.6%) reported to have the higher prevalence of self-reported asthma compared to others age groups and all were currently on medications (Table I).

All participants who had symptoms of asthma based on the IUATLD questionnaire, self-reported asthma or currently on medication were confirmed by lung function test (spirometry) to having bronchial asthma with overall prevalence of 1.4% (10 of 716). Of these, 1.5% (8 of 549) and 1.2% (2 of 167) were children and adults, respectively (Table II). With regards to gender, prevalence of bronchial asthma was slightly higher in female (1.7%, 7 of 412) compared to male (1.0%, 3 of 304). Of the eight subgroups surveyed, five out of ten confirmed asthma cases were among Semai Pahang subgroup, followed by three cases among Mah Meri subgroup, and one case each among Temuan and Semai Perak subgroups, respectively. Due to low number of bronchial asthma cases (10 out of 716) in this study hence, no statistical analysis were applicable.

The potential risk factors associated with asthma were explored as shown in Table III. It clearly demonstrated that the prevalence of self-reported (6.2%) and confirmed bronchial asthma (1.5%) were higher among those had close contact with pets. In addition, both prevalence of self-reported (9.3%) and bronchial asthma (1.9%) were also slightly higher among smoking individuals compared to non-smoking individuals. The prevalence was also reported higher among those who had a family history of asthma in both self-reported (46.7%) and confirmed bronchial asthma cases (10.0%), respectively.

DISCUSSION

The results of the IUATLD questionnaire demonstrated that 6.4% and 10.6% of the participants had symptoms of wheezing and coughs in the past 12 months, respectively. In addition, 6.0% of the participants of the study had self-reported asthma. The IUATLD questionnaire on wheezing, cough and self-reported asthma was used to screen for the possible presence of asthma following spirometric testing, the results of which were validated by a consultant respiratory physician of UMMC with 1.4% of the participants confirmed to have bronchial asthma. To date, there is a scarcity of information on the respiratory status (e.g. asthma) among the Orang Asli in Malaysia. Moreover, there is no publication on population-based studies on asthma among the Orang Asli and only sporadic compilations of limited hospitalized data by the Disease Control Division, Department of Public Health, Ministry of Health (MOH) Malaysia among this community. To the best of our knowledge, this is the first reported cases of bronchial asthma based on the clinical interpretation among this community in Malaysia.

These findings showed that the prevalence of asthma was low among the Orang Asli communities living in the rural areas of Peninsular Malaysia. According to statistics from the Disease Control Division, Department of Public Health, MOH Malaysia, the prevalence of hospitalization of severe asthma cases among the Orang Asli from the year 2000 to 2005 was very low, with a mean of 0.02%⁸. Currently, more than 130 million people worldwide suffer from asthma and the number is increasing especially in Western industrialized countries compared to less develop or developing countries⁹. In Malaysia, asthma is among the commonest medical conditions giving rise to considerable morbidity and mortality with an estimation of 1.6 to 2 million cases among the Malaysian general population⁶.

A local study found that 13.8% of primary school children in Kuala Lumpur to be asthmatic¹⁰. Asthma is under diagnosed and often not managed optimally. In an ongoing surveillance of paediatric asthma deaths, nine death have been reported and all of them have been due to inadequate assessment of the severity of the attack and hence under treatment¹⁰. There is an over reliance on symptomatic and oral therapy leading to inadequate control and in some cases, death. It is also recognized that disparities in management exist due to lack of access to appropriate information, drugs and resources¹¹.

It has been suggested that people living in rural areas generally report better health, are less likely to be disabled or suffer from a long-term limiting illness including asthma. There was also strong evidence of differences in the prevalence of allergic diseases including asthma between rural and urban areas within a country, with a higher prevalence of allergic diseases reported in urban areas^{9,12,13}. Report from a cross-sectional study in Scotland showed that people living in a rural area was associated with a lower prevalence of asthma compared to urban residency¹⁴. In the United Kingdom, exercise-induced bronchospasm among Highland schoolchildren was found to be significantly higher in one of the most rural areas studied (Skye) compared with the rest of the United Kingdom or other areas in the Highlands¹⁵. Others

Table I: Symptoms of wheezing and coughing in the last 12 months, self-reported and confirmed asthma according to age subgroups

Age (year)	N	Wheezing		Coughing		Self-reported asthma		Confirmed bronchial asthma	
		No.	%	No.	%	No.	%	No.	%
1-4	7	0	0	3	42.9	0	0	0	0
5-6	17	1	5.9	5	29.4	3	17.6	0	0
7-12	525	33	6.3	51	9.7	32	6.1	8	1.5
13-17	15	0	0	1	6.7	0	0	0	0
> 18	152	11	7.2	16	10.5	8	5.3	2	1.3
Total	716	45	6.3	76	10.6	43	6.0	10	1.4

N: number examined; No: number positive case; %: percentage positive case

Table II: Confirmed bronchial asthma cases based on spirometry by age groups and gender

Variables	N	Confirmed bronchial asthma	
		No.	%
Age groups			
Children (≤ 12 years)	549	8	1.5
Adults (≥ 12 years)	167	2	1.2
Gender			
Male	304	3	1.0
Female	412	7	1.7
Total	716	10	1.4

N: number examined; No: number positive case; %: percentage positive case

Table III: Potential risk factors associated with self-reported asthma and confirmed bronchial asthma

Variables	N	Self-reported asthma		Confirmed bronchial asthma	
		No.	%	No.	%
Close contact with pets					
Yes	601	37	6.2	9	1.5
No	115	6	5.2	1	0.9
*Smoking					
Yes	54	5	9.3	1	1.9
No	112	3	2.7	1	0.9
Family history					
Yes	30	14	46.7	3	10
No	686	29	4.2	7	1.2

N: number examined; No: number positive; %: percentage positive case

* Total number examined was based on total number of smoker

have found that wheeze in the past year, both with and without a diagnosis of asthma was lower in rural compared with urban areas¹⁶.

The prevalence of bronchial asthma among the Orang Asli living in rural and remote areas was lower than the prevalence of asthma (ranging from 2.1% to 32.2%) from 155 centers in 56 countries that participated in the ISAAC study². In addition, study on the prevalence of asthma among indigenous communities in Australia found that 16.0% participants reported ever had asthma¹⁷ compared to 6.0% self-reported asthma in the present study. This difference may be partly due to the differences in the study methodology. Most of the study on the prevalence of asthma relied on self-reported symptoms information based on questionnaire interview and could have been affected by information biasness whereas our study was based on a combination of both questionnaire and pulmonary function test. An Australian study among middle-aged and older adults found little difference between the self-reported prevalence of asthma, chronic bronchitis and emphysema, and the prevalence of these conditions confirmed by a doctor¹⁸.

The low prevalence of bronchial asthma among Orang Asli communities could also partly be due to their living conditions and personal hygiene. There is some evidence that if the immune system is exposed to high levels of allergen, as might be the case in rural settings, a form of immune tolerance may occur, perhaps resulting in less allergic disease²⁰. It has been proposed that the lack of intense infections in urban area owing to improved hygiene, vaccination and use of antibiotics may alter the human immune system such that it responds inappropriately to innocuous substances²¹. Taken together these observations suggest an inverse relationship between high living standard and hygiene conditions with an increased risk to develop an allergic disease²². The idea is part of a broader hypothesis suggesting that exposure to infections in early childhood reduces the risk of developing allergies, the so-called 'hygiene hypothesis'. The "hygiene hypothesis" was originally proposed by Strachan in 1989 when he observed a higher prevalence of allergic disease in first born children compared to their younger siblings²³.

The present study also demonstrated the significant role of lung function test in the assessment of asthma which 6.0%

cases of self-reported asthma, however only 1.4% were confirmed by physician as a bronchial asthma after lung function test. This findings support the recommendation that lung function test is crucial in the assessment of asthma severity²⁴. One important reason for this recommendation is that in chronic diseases such as asthma, patients tend to downplay the severity of their symptoms, leading to under-appreciation of the true disease severity and commonly under-treatment. As such, lung function test can provide an objective assessment to the attending clinician, and ensure appropriate treatment. Another reason is the recognition of poor correlation between reported symptoms and physiologic measurement or airway caliber such as FEV₁ in many asthmatic patients. Poor perceptions of symptoms in particular, increase the risk for under-treatment and possibly fatal asthma attack²⁴.

In addition, the study attempted to examine the effect of other common risk factors for asthma such as family history of asthma, smoking habits and presence of domestic animals at home. However, no statistical analysis was applicable due to the low number of bronchial asthma in the present study limiting the statistical power of this study to examine further association between risk factor relating to asthma. Although smoking did not significantly increase the risk of asthma, it was observed that asthma was slightly more common among smoking adults as compared to non-smoking individuals. There was also higher number of asthma cases among those who had a positive family history. Liu and co-authors²⁵ found that persons with a family history of asthma are up to six times more likely to develop the disease than normal person. These findings show that a family history of asthma is an important risk factor for asthma and that risk assessment based on this variable can help identify people at higher risk of developing asthma.

CONCLUSION

It is concluded that the prevalence of asthma among the Orang Asli is low. Our results highlight the importance of spirometry in confirming the true prevalence of asthma as there is a potential for the misdiagnosis of asthma based on questionnaire survey.

ACKNOWLEDGEMENT

The authors are very grateful to the Director of Department of Orang Asli Affair (JHEOA), Ministry of Rural Development, Malaysia for giving permission to conduct this study among various Orang Asli communities. Special thanks also go to Mr. Saidon Ishak, Mr. Wan Hafiz Wan Ismail and Mr. Shukri Jaafar for their technical assistance. Most importantly, the authors would like to thank all the eight Orang Asli subgroups who have voluntarily participated in this study.

REFERENCES

1. Lai CKW, de Guia TS, Kim YY, *et al.* Asthma control in the Asia-Pacific region: The Asthma insights and reality in Asia-Pacific study. *J Allergy Clin Immunol* 2003; 111: 263-68.
2. ISAAC. The International Study of Asthma and Allergies in Childhood Steering Committee. Worldwide variations in the prevalence of asthma symptoms: The International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998; 12: 315-35.
3. Kim YY, Cho SH, Kim WK, *et al.* Prevalence of childhood asthma based on questionnaires and methacholine bronchial provocation test in Korea. *Clin Exp Allergy* 1997; 27: 761-68.
4. Bahari MB, Mohd Nur M, Rahman FAB. A knowledge of asthma in school children: A survey among primary school teachers. *Singapore Med J* 2003; 44: 131-35.
5. Rozlan I. The study on asthma admissions in Malaysia. *Disease Control Division (NCD), Ministry of Health Malaysia* 2002; 1: 10-17.
6. Bakri R, Mohd Said N, Mohan J, *et al.* National Health and Morbidity Survey. Ministry of Health, Malaysia 1999.
7. Burney PGJ, Laitinen LA, Perdrizet S, *et al.* Validity and repeatability of the IUATLD (1984) Bronchial Symptoms Questionnaire: an international comparison. *Eur Respir J* 1989; 2: 940-45.
8. Ministry of Health (MOH). Disease Control Division, Department of Public Health, Ministry of Health, Malaysia 2007.
9. Yemaneberhan H, Bekele Z, Venn A, *et al.* Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. *Lancet* 1997; 350: 85-90.
10. Azizi HO. Respiratory symptoms and asthma in primary school children in Kuala Lumpur. *Acta Paediatr Japon* 1990; 32: 183-87.
11. Azizi HO, Lee EL, Mohan J, *et al.* Guidelines for the management of childhood asthma. *Medical Journal of Malaysia* 1997; 52: 416-27.
12. Scrivener S, Yemaneberhan H, Zebenigus M, *et al.* Independent effects of intestinal parasite infection and domestic allergen exposure on risk of wheeze in Ethiopia: a nested case-control study. *Lancet* 2001; 358: 1493-99.
13. Dagoye D, Bekele Z, Woldemichael K, *et al.* Wheezing, allergy, and parasite infection in children in urban and rural Ethiopia. *Am J Respir Crit Care Med* 2003; 167: 1369-73.
14. Iversen L, Hannaford PC, Price DB, *et al.* Is living in a rural area good for your respiratory health? Results from a Cross-sectional study in Scotland. *Chest* 2005; 128: 2059-67.
15. Austin JB, Kaur B, Anderson HR, *et al.* Hay fever, eczema, and wheeze: A nationwide UK study (ISACC, international study of asthma and allergies in childhood). *Arch Dis Child* 1999; 81: 225-30.
16. Court, CS, Cook, DG, Strachan, DP. Comparative epidemiology of atopic and non-atopic wheeze and diagnosed asthma in a national sample of English adults. *Thorax* 2002; 57: 951-57.
17. Valery PC, Chang AB, Shibasaki S, *et al.* High prevalence of asthma in five remote indigenous communities in Australia. *Eur Respir J* 2001; 17: 1089-96.
18. Abramson M, Matheson M, Wharton C, *et al.* Prevalence of respiratory symptoms related to chronic obstructive pulmonary disease and asthma among middle aged and older adults. *Respirology* 2002; 7: 325-31.
19. Senthilselvan A, Dosman JA, Chen Y. Relationship between pulmonary test variables and asthma and wheezing: a validation of self-report of asthma. *J Asthma* 1993; 30: 185-93.
20. Platts-Mills, TA, Vaughan, JW, Blumenthal, K, *et al.* Serum IgG and IgG4 antibodies to Fel d 1 among children exposed to 20 microg Fel d 1 at home: Relevance of a nonallergic modified Th2 response. *Int Arch Allergy Immunol* 2001; 124: 126-29.
21. Helmby H. Helminths and our immune system: Friend of foe? *Parasitol Int* 2009; 58: 121-27.
22. Garn H, Renz H. Epidemiological and immunological evidence for the hygiene hypothesis. *Immunobiology* 2007; 212: 441-52.
23. Strachan DP. Hay fever, hygiene and household size. *Br Med J* 1989; 299: 692-95.
24. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention, updated 2009. www.ginasthma.org.
25. Liu T, Valdez R, Yoon PW, *et al.* The association between family history of asthma and the prevalence of asthma among US adults: National Health and Nutrition Examination Survey, 1999-2004. *Genet Med* 2008; 11: 323-28.